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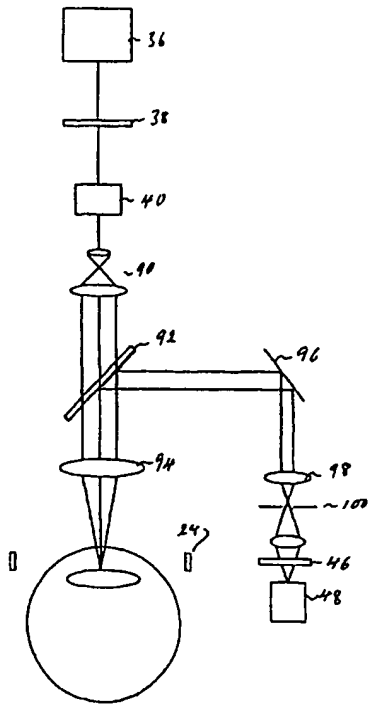

(57) Abstract: A non-invasive apparatus and method of optically sensing the glucose concentration of a solution is provided. The optical glucose sensor (10) is based on the fact that glucose solutions have a magnetic optical rotatory effect (MORE) such that when a magnetic

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field is set up in a glucose solution there is a rotation of the polarization vector of the incident light that is proportional to the path length, magnetic field strength, and the concentration of glucose in the solution. The optical glucose sensor (10) includes a laser (36) that passes a beam of polarized light (12) through the glucose solution (i.e aqueous humor or an eye) while a coil (24) sets up a magnetic field (B) in the solution. A photomultiplier tube (48) provides an output signal indicative of the rotation of the polarization vector of incident light. The beam of light (12) is also modulated by a Faraday rotator (46), which is controlled by a lock-in amplifier (52) that closes a feed back loop. The output of the lock-in amplifier (52) generates a signal indicative of the glucose concentration in the solution, which may be displayed on an oscilloscope (60) or provided to a processor, which displays a readout indicative of the glucose concentration.

OPTICAL GLUCOSE SENSOR APPARATUS AND METHOD

FIELD OF THE INVENTION

The present invention relates to apparatus and methods of determining the glucose concentration of a glucose solution and more particularly, to an apparatus and method for non-invasive testing of the blood glucose of an individual based on measuring the optical rotation of glucose in the aqueous humor of the eye by optical methods.

BACKGROUND OF THE INVENTION

Diabetes mellitus represents one of the major health problems today. Often, diabetes leads to such problems as renal failure and vision impairment. Estimated costs of diabetes related health care range between $20 to $40 billion annually. However, a recent multi-center NIH study has indicated that the health risks associated with diabetes are significantly reduced when the blood glucose levels are tightly controlled, indicating that it is prudent to measures the blood glucose as often as five or six times a day. Thus it is important that proper monitoring be done by diabetics at home or work.

Presently, existing methods of home blood glucose monitoring require obtaining a blood sample by pricking the fingertip with a needle or lancet (referred to as a "stick"), allowing the puncture to bleed until a testing strip is adequately covered with blood, and then placing the coated strip into a glucose monitor for testing. This method strongly discourages patient compliance and has the following serious drawbacks. First, this procedure is invasive. For many people, the prospect of performing 5 or 6 "sticks" daily is intimidating and painful. In addition, it provides a significant opportunity for infection for a population, which is pre-disposed to infection of the extremities.

Second, this procedure for testing is laborious and involved. Many people have trouble learning how to test their own blood glucose. In addition, the procedure can become a nuisance, since it requires thorough hygiene (washing the hands, cleaning the area which is to be "stuck", etc.) and an involved testing procedure using strips and monitoring devices in the exact same manner. Third, there is little margin for error in the testing procedure, and thus many individuals do not necessarily obtain accurate results due to poor testing practices. Fourth, this procedure is expensive. Although the current marketing strategy employed by most manufacturers is to sell the monitor rather cheaply, the testing remains expensive and is the real source of profit, routinely costing 80 cents each. Thus tight blood sugar controls, requiring 5 or 6 strips daily, can cost patients over $1,000 annually.

Alternatively, a non-invasive method of testing an individual's blood glucose presently exists. This non-invasive method reflects a beam of light through the aqueous humor glucose. The method measures the polarization rotation of the beam to determine the concentration of the blood glucose.

Problems with previous noninvasive optical glucose measuring devices include the lack of spatial resolution of the rotatory effect, i.e. all tissues traversed by the beam affect the rotatory status of the light field. Second, the signal-to-noise ratio of optical rotatory effect is limited by the DC frequency of the conventional rotatory effect. Third, conventional optical rotatory effect is cancelled upon reflection from a dielectric mirror surface (the aqueous/lens interface is an example of such a surface). Thus, US-A-3958560 discloses a glucose concentration measurement performed by passing light across the anterior chamber of the eye and detecting the rotation of the polarization vector of the light. However, the scheme requires an extreme and essentially impractical degree of miniaturization of the apparatus having regard to the constraints posed by the size of the eye and facial features.

US-A-5535743 attempts to overcome these problems by proposing the projection of a polarized beam of light onto the anterior face of the lens of the eye at an angle to the normal and the reflection of the light beam at an equal and opposite

angle to the normal so that the light traverses twice through the anterior chamber and its aqueous humor. The problem that will be caused by the cancellation of the optical rotation produced by passage through the aqueous humor of the incident beam when opposite rotation is produced in the reflected beam as it passes out through the aqueous humor is not recognized or addressed. We have appreciated that in practice, no measurable rotation will be observed.

US-A-5535743 discloses the use of a Faraday rotator in the light path to modulate the polarization of the light coupled with a lock in amplifier to improve the suppression of noise in the detection of the rotation.

EP-A-0805352 discloses a polarimetric method of determining the concentration of glucose in urine to which polarized light is passed through a Faraday rotator and then through a sample cell to a light sensor. It is further disclosed that the solenoid coil may be provided surrounding the sample cell so that the current needed in the coil to negate the optical rotation of the polarized light by the urine may be measured. In this arrangement, there is no recognition that the Verdet constant of glucose solution will be a function of the glucose concentration and no use is made of this phenomenon.

SUMMARY OF THE INVENTION

In accordance with the present invention, an apparatus for determining the concentration of optically active substances in a solution comprises a laser for producing a beam of light. The beam of light passes through a coil having a predetermined number of turns. The coil is disposed about at least a portion of the solution, preferably the aqueous humor of an eye. An alternating current source is electrically connected to the coil to generate a magnetic field through the solution disposed therein. An optical detector receives the beam of light after the beam passes through the portion of the solution and the coil. The optical detector provides an output signal indicative of the optical rotation of the solution, wherein the optical rotation is proportional to the concentration of the optically active substance.

In accordance with another embodiment of the present invention, a method for optically sensing concentration of optically active substance in a solution comprises generating a polarized beam of light and passing the beam through the solution. A magnetic field is set up through the solution to provide a polarization of the vector of incident light, which is proportional to the concentration of the optically active substance in the solution. The rotation of the polarization of the received polarized beam of light is determined.

According to another aspect of the invention, there is provided a method for measuring the concentration of a material in aqueous humor of an eye, comprising the steps of generating a beam of polarized light from a light source; directing said beam into an eye of a subject along a light path such that the beam reflects from an interface in the eye and returns from the eye back towards the light source; applying a modulated gyrotropic field to the aqueous humor of the eye which gyrotropic field is effective to produce an alteration in the polarization of the light passing through the aqueous humor in the field which alteration may be represented as $\delta = B x f(C_m) x d$, where δ is the alteration in polarization, B is the field strength, C_m is the concentration of the material, $f(C_m)$ is a function of the said concentration, and d is the distance traversed to produce a modulated alteration in the polarization of the reflected beam of light related to the intensity of the gyrotropic field and the dependence of said function $f(C_m)$ on the concentration of said substance within the aqueous humor; receiving the reflected beam of light and detecting said modulated variation in polarization; and determining the concentration of said substance from said alteration in polarization produced by said field dependent on the concentration related value of the function $f(C_m)$.

The gyrotropic field may be any field which acting on the medium in which the measurement is being made (e.g. the aqueous humor of the eye) produces a rotation of the polarization vector of the light in a field dependent manner which further is a function of the concentration of the material of which the concentration is to be measured. The field is preferably a magnetic field and the amount of rotation of the polarization vector of the light produced for a given field strength then depends on the Verdet constant of the medium which (despite the name Verdet constant) will be a function of the concentration of the material to be measured.

The gyrotropic field may alternatively in an appropriate case be an electric field.

The interface from which the light is reflected in the eye is preferably the anterior surface of the lens of the eye but could be the posterior surface of the lens, the iris, the retina, or the white of the eye.

The polarization of the light used in the method of the invention may be linear or circular but is preferably linear.

Although the magnetic field is preferably produced by a coil positioned in proximity to the eye, a permanent magnet may be used and variations in the magnetic field experienced within the aqueous humor may be produced in various ways including movement of the magnet itself or of a shield which shields the aqueous humor from the magnetic field to a varying degree according to its position.

The shield may be a second magnet or may be of material serving to block magnetic field lines such as mu metal.

Where a coil is the source of the field, the current driving the coil may have a DC component.

A combination of a coil and a permanent magnet may be used.

The light is preferably reflected back along substantially the same path by which it reached the interface in the eye, preferably the angle between the incident beam and the reflected beam is 0° but it may be up to 30°, more preferably up to 10°.

According to yet another aspect of the invention, there is provided apparatus for optically measuring the concentration of an optically active material in the aqueous humor of an eye, comprising a light source generating a beam of polarized light; said source being mounted to direct said beam into an eye of a subject along a light path such that the beam reflects from the anterior surface of the lens of the eye and returns from the eye towards the light source, a source of a modulated gyrotropic field adapted to be located sufficiently close to the aqueous humor of the eye to produce a modulated alteration in the polarization of the beam of light, which

gyrotropic field is effective to produce an alteration in the polarization of the light passing through the aqueous humor in the field which alteration may be represented as $\delta = Bxf(C_m)xd$, where δ is the alteration in polarization, B is the field strength, C_m is the concentration of the material, $f(C_m)$ is a function of the said concentration, and d is the distance traversed to produce a said modulated alteration in the polarization of the reflected beam of light related to the intensity of the gyrotropic field and the dependence of said function $f(C_m)$ on the concentration of said substance within the aqueous humor; an optical detector for receiving the reflected beam of light and detecting said modulated alteration in polarization; and computation apparatus for determining the concentration of said substance form said alteration in polarization produced by said field dependent on the concentration related value of the function $f(C_m)$.

There is further provided an apparatus for determining the concentration of an optically active substance in a solution, the apparatus comprising a light source for producing a beam of light arranged to direct said beam of light to pass through at least a portion of said solution; a source of magnetic field applied to at least said portion of the solution; an optical reflector arranged with respect to said light source and said solution so as to reflect said beam of light to re-pass through at least said portion of said solution; an optical detector for receiving said beam of light after said re-passage through the solution in the presence of the magnetic field.

According to yet a further aspect of the invention there is provided a method for measuring the concentration of a substance in a solution, comprising the steps of measuring magneto-optical rotation produced in said solution, which rotation is indicative of the concentration dependent Verdet constant of the solution, and obtaining said concentration therefrom.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described, by way of example only, with reference to the accompanying drawings in which:

Figure 1 is a functional diagram of an optical glucose sensor embodying the present invention;

Figure 2 is a diagrammatic view illustrative of reflective characteristics from a dielectric mirror of light passing through an optical rotatory medium;

Figure 3 is a diagrammatic view illustrative of reflective characteristics from a dielectric mirror of light passing through a magnetic optical rotatory effect cell embodying the present invention;

Figure 4 is an enlarged diagrammatic view of an eye with a detector beam reflecting off the aqueous humor passing through a magnetic field provided by the optical glucose sensor of Figure 1;

Figure 5 is a graphical illustration of the voltage output of the optical glucose sensor of Figure 1 for a single pass through the MORE cell;

Figure 6 is a graphical illustration of the voltage output of the optical glucose sensor of Figure 1 for a double pass through the MORE cell;

Figure 7 is a functional diagram of an alternative embodiment of an optical glucose sensor embodying the present invention;

Figure 8 shows the layout of optical components in a further preferred apparatus according to the invention; and

Figure 9 shows the layout of optical components in a further preferred apparatus according to the invention.

DETAILED DESCRIPTION OF THE INVENTION

Referring to Figure 1, a non-invasive optical glucose sensor 10 embodying the present invention is illustrated. The glucose sensor 10 passes a beam of polarized light 12 through a glucose solution 14, which is reflected back through

the solution. The glucose solution has a Faraday effect, thus providing an optical rotatory medium (e.g., Faraday Rotator) that rotates the polarization of light passing therethrough. The optical sensor 10 measures the polarization rotation of the reflected beam of light after passing through the glucose solution 14. It has been found that when a magnetic field (B) is set up in the glucose solution there is a rotation of the polarization of the vector of the incident light that is proportional to the path length, magnetic field strength and the concentration of the glucose in the solution. This relationship between the glucose concentration of the solution 14 and the rotation of the polarized light 12 passing therethrough permits non-invasive measurement of the glucose contrention of the solution. This magnetic optical rotatory effect (MORE) of a glucose solution 14 was found to be linearly proportional with the glucose concentration with a negative slope at physiologic concentrations, as will be described hereinafter.

Figure 2 illustrates the reflection of a beam of light 12 passing through a cell of an optical rotatory medium 14 (i.e., a glucose solution) and reflecting back therethrough off a reflective surface 16, such as a dielectric surface. The geometry of the passage of the polarized beam 12 reflected through the cell 14 is shown graphically by the vector of the electric field (E) 18. The direction of the E vector of the transmitted beam is shown at 20. The effect of the beam of light 12 reflected from the dielectric mirror 16 is similar to that of a conventional optical rotatory effect as is well know in the art. Generally, the resulting rotation of the **E** vector 16, as shown at 22, is 180°, and thus cancels the reflection resulting in zero net optical rotation. Graphically shown at 20 and 22, the direction of rotation is given by **k x E**, and both **k** and **E** show no net rotation of the reflective beam. This cancellation of the conventional optical rotatory effect upon reflection from a dielectric mirror surface is discussed in the article "Polarimetry in the Presence of Chiral and Gyrotropic Media and Various Reflection and Retrodirection Mirroring" published in Journal of Electromagnetic Waves and Applications, v.11 297-313, 1997, which is hereinafter incorporated by reference.

Figure 3 illustrates the reflection of a beam of light 12 through a cell 14 of a similar optical medium, as shown in Figure 2, wherein a magnetic field (B) is set up in the optical rotatory medium by conducting an alternating current through the coil 24 disposed about the medium. In contrast to the method illustrated in Figure 2, the cell of Figure 3 uses the magnetic Optical Rotator Effect ("MORE") to achieve double the rotation (2θ) in the same geometry. This double rotation is achieved because the direction of rotation is dependent on the vector cross product B x E, and the direction of B remains in the same direction as indicated by arrows 26. The direction of the E vector 18 of the transmitted beam is shown at 28. As shown, the reflection of the light beam 12 from the dielectric mirror 16 and magnetic optical rotatory effect cell 14 with glucose solution results in 180 degree rotation of E vector 18 (due to the mirror reflection) with an additional 2θ phase shift, as shown at 30. This method eliminates the cancellation of the conventional optical rotation effect that occurs upon reflection from a dielectric [E field inverting] mirror.

This method of optically sensing the concentration of glucose in a solution 14 disposed in the aqueous humor 31 in accordance with the present invention may be used to provide a non-invasive procedure to determine the glucose level of an individual by reflecting the beam of light 12 off the lens 32 in the human eye 34 as illustrated in Figure 4. The lens/aqueous interface can be characterized as a dielectric mirror 16. For such an interface, the magnetic optical rotation effect should double the detected rotation. The double rotation is due to the light beam 12 passing twice through the glucose in the aqueous humor 14 with magnetic field (B) after reflection of the light beam 12 from the aqueous/lens interface.

Referring again to Figure 1, a detailed description of the optical glucose sensor 10 is provided. The sensor is similar in a number aspects as that disclosed in the articles "Multiple Wavelength Non-Invasive Ocular Polarimetry for Glucose Measurement for Managing of Diabetes", published in SBIR Program Final Report, 1995; and "Optical Glucose Sensor Using a Single Faraday Rotator, published in Proceedings of the 23rd Annual Northeast Bioengineering Conference, May 21-22, 1997; each of which are hereinafter incorporated by reference. A coherent light

source 36, currently a helium neon (HeNe) laser, emits a collimated beam 12. This could be a laser operating at a different frequency (i.e., infrared diode) or a coherent light source with a collimating lens. In the alternative, the light source may be a white light source. The light from such a white light source should preferably be made monochromatic by the use of suitable filters or a diffraction grating. Other suitable non-temporally coherent light sources include led's, incandescent light bulbs, and gas discharge lamps, for instance a sodium lamp, a deuterium lamp, an iodine quartz lamp or a xenon flash lamp. The light frequency employed in the invention may be selected to be especially eye-safe, being a frequency which is well absorbed in the vitreous humor and which will therefore be attenuated before it reaches the retina. Measurements may be carried out at two or more light frequencies so as to enable the elimination of the effects of confounder substances present in the aqueous humor by virtue of the difference in the light frequency dependency of their $f(C_m)$. Multiple light frequencies may be used. The beam 12 is then passed through a first polarizer (P1) 38, which linearly polarizes the light of the beam to produce a field (E). The laser 36 provides approximately 2 mW effective output after the first polarizer 38 of 633 nm.

The light beam 12 then passes through a Faraday rotator (FR) 40 which rotates the polarization of the beam approximately 5°. This degree of rotation is dependent on the level of the voltage, which may be increased by increasing the voltage provided to the Faraday rotator. One skilled in the art will know that a poeckel cells, liquid crystals and kerr cell may also be used to rotate the polarization of the beam. A function generator 42 provides an approximately 1.2 kHz drive signal to the Faraday rotator 40. The light beam 12 then passes through the cell 14 (MORE cell) of glucose solution (e.g., the aqueous solution of the aqueous humor 31) and reflects back through the cell, as shown in Figure 3. A coil 24 of a predetermined number of turns is electrically connected to an alternating current (ac) source 44. The number of turns of the coil is based on the desired magnitude of the magnetic field (B). In one embodiment, the number of turns is greater than 100. The frequency of the ac source, for example, may be approximately 10 Hz, however, one skilled in the art will appreciate that signal to noise ratio improves as the frequency of the ac source

increases. The coil 24 winds about the cell 14, such that the longitudinal axis of the coil is generally perpendicular to the reflective interface 16. The ac source 44 and the coil 24 generate a magnetic field (B) throughout the glucose solution, which can be precisely controlled. In a one embodiment of the present invention, the inner diameter of the coil 24 is substantially equal to the diameter of the human eye (i.e., the cell). In the operation of the optical sensor 10, the coil 24 is place within the user's eye socket so that a portion of the eye 34 is disposed within the coil. The reflected beam 12 then passes through the coil and the glucose solution of the aqueous humor 31 within the eye 34 and reflects off the lens 32 and back through the solution and coil.

The light beam 12 then passes through a second polarizer (P2) 46, which is disposed at 90 degrees to the first polarizer 38. The resulting rotation of the polarized beam passing through the second polarizer 46 is determined by a photomultiplier tube (PMT) 48 that generates an electrical output signal at lead 50 representative of the rotational position of the beam 12. The output signal is fed back to the Faraday rotator 40 through a lock-in or phase lock amplifier 52, an electronic circuit 54 and a two (2) Henry inductor 56 to close the loop. The output signal is also provided to an oscilloscope 60 via lead 58 for displaying the output signal. In the alternative, the output signal from the photomultiplier tube 48 and the lock-in amplifier 52 may be provided to a processor that generates a phase signal indicative of the phase rotation of the glucose in the aqueous humor 31. The phase signal is provided to a readout, which displays a result indicative of the concentration of the glucose in the aqueous humor.

The lock-in amplifier 52 provides an output signal, which is a dc voltage proportional to the amplitude of the 1.2 kHz present in the output signal from the photomultiplier 48. This dc output voltage is fed back to an integrator of the electronic circuit 54 and the Faraday rotator 40 through the inductor 56 to close the loop. The lock-in amplifier 52 therefore provides phase and frequency locked detection of the 1.2 kHz component, which is proportional to the net rotation between the two polarizers 38 and 46 disposed at 90° to each other. The bandpass of the

feedback loop also limits the lock-in frequency. As described hereinbefore, increasing the lock in frequency increase the signal to noise ratio of the system. The MORE cell 14, varies or modulates this net rotation at the frequency of the magnetic field (B), which may be set at approximately 10 Hz (frequency of the ac source 44). The resultant signal is picked up as a 10 Hz p-p ac signal on the oscilloscope 60. The function generator also provides the 1.2 kHz signal to the lock-in amplifier. This AC modulation of the desired signal, which can be detected using the lock-in amplifier 52 for phase coherent detection, results in improved signal to noise ratio. This lock-in technique can actually pull a signal out of over 100 db of additive random noise.

In the sensing of the glucose level of the glucose solution with the aqueous humor 31 of the eye 34, the beam of light 12 passes through the magnetic optical rotatory cell 14 after reflection from the dielectric mirror 16, the magnitude of rotation due to the MORE cell is proportional to the concentration of the glucose, the path length of the cell, and the magnitude of the magnetic field (B) in the cell.

In an alternative embodiment, a single magnetic optical rotatory effect (MORE) cell may be used to sense the optical rotation of a glucose solution. A single MORE cell is similar to that described hereinabove except the light 12 is not reflected back through the cell 14 (glucose solution), but reflected directly to the second polarizer 46.

Figures 5 and 6 illustrate graphically the peak to peak voltage of the output signal of the optical sensor 10 versus the glucose concentration of the solution for a single MORE cell and double MORE cell, respectively. The output slopes 66, 68 for both single and double MORE, respectively, are shown in equations (1) and (2) below:

$$\left|\frac{\Delta Vp-p(mV)}{\Delta G(mg/dl)}\right|_{1MORE} = 0.242\,(mV/(mg/dl)) \qquad (1)$$

$$\left|\frac{\Delta Vp-p(mV)}{\Delta G(mg/dl)}\right|_{2MORE} = 0.476\,(mV/(mg/dl)) \qquad (2)$$

Where Vp-p is peak-peak voltage output is from the lock-in amplifier 52; and
G is the concentration of glucose solution in mg/dl.

As shown by equations (1) and (2), the double MORE cell provides twice the optical rotation of the single pass of the single MORE cell, and thus showing that the double MORE had 99.7% greater slope (close to the predicted 100% greater slope) indicating twice the sensitivity of single MORE cell.

Referring to Figure 7, an alternative embodiment of an optical glucose sensor 70 is shown. Like numbered components of the sensor 10 illustrated in Figure 1 and described hereinbefore are similar to sensor 70 shown in Figure 7. The glucose sensor 70 of Figure 7 further includes an additional lock in amplifier 72 for a second feedback loop to improve the signal to noise ratio of the sensor. The output signal of the first lock in amplifier 52 is provided to the input of the second lock in amplifier 70. Further, the ac source 44 is provided to the input of the second lock in amplifier 70. The output of the second lock in amplifier is then provided to the oscilloscope 60 (or processor).

As the amount of optical rotation produced by the Faraday effect in the sample depends on the concentration of the detected substance and upon the intensity of the magnetic field, an alternative detection strategy is to vary the maximum intensity of the field by adjustment of the ac voltage/current applied to the coil in Figure 7 to produce a predetermined level of optical rotation and to use the current applied to the coil or the current flowing in it as a measure of the concentration. As an alternative to providing the Faraday rotator 40 and coupling the lock in amplifier to

it, the lock in amplifier may instead be coupled to the ac source 44, and the Faraday rotator 40 may be omitted.

Figure 8 shows apparatus for measuring the concentration of a substance such as glucose within the aqueous humor of the eye, in which the optical components described previously are arranged in a preferred optical geometry. The light source 36 directed through the polarizer 38 and through the Faraday rotator 40, as in Figure 1. A half silvered mirror M1 is interposed between the Faraday rotator 40 and the eye. Coil 24 is arranged surrounding the front of the eye. The light beam 12 enters the eye normal to the anterior surface of the lens via the aqueous humor and is reflected back along the same path to the mirror M1 from which it is reflected to a second mirror M2 and from there to the second polarizer 46 to the optical detector 48. The electronic components are connected to the optical components as shown in Figure 1 or Figure 7.

Figure 9 shows a further preferred optical geometry. Light from a light source 36 is directed through a linear polarizer 38 and a Faraday rotator 40 and then to a beam spreader and spatial filter 90. The broadened beam then passes through a glass plate 92, the right hand half of which is silvered on the face nearer the eye. Thus only the left hand part of the broadened beam is passed on and the right hand half is blocked. There is then a lens system 94 focusing the beam on the anterior surface of the eye lens. The solenoid coil 24 surrounds the front of the eye. Light reflected from the eye lens is directed back toward the light source and is spread by the lens system 94 before impinging on the plate 92. That part of the reflected light falling on the silvered part of the plate is reflected across to a mirror 96 and via a lens 98 and an aperture plate 100 to a polarizer 46 and to the photodetector 48.

The use of the part silvered plate 92 and the focusing of the reflected light through the aperture plate 100 serves to exclude reflections from other interfaces in the eye such as the surfaces of the cornea from reaching the photodetector.

Advantages of this arrangement over that in which the light is incident on the lens at an angle off the normal and is reflected therefrom at an equal angel to the opposite side of the normal plane are that complexities in the effect of reflection on the polarization of the light are reduced by the absence of light components parallel to the reflecting surface and the apparatus is made physically easier to align and to focus on the desired reflecting surface. Adjustment for differing optical characteristics of different eyes may be made by movement of one component, namely the lens system 94.

In these embodiments and more generally in accordance with the invention, the magneto-optical rotation which is measured is that produced by the Faraday effect as the light passes through a solution of a substance whose concentration is to be measured and the amount of rotation is determined by the variation with concentration of said substance of the Verdet constant of the solution for the light wavelength used. This is in contradistinction to what is seen in EP-A-0805352, where the normal optical rotation of the urine is measured using the Faraday effect magneto-optical rotation merely as a tool for assisting measurement of the conventional optical rotation of the solution.

The present invention described hereinbefore for optically sensing glucose using the fact that magnetically induced optical rotation in glucose solutions is linearly proportional to glucose concentration at physiologic levels has many advantages over the prior art. This non-invasive method of testing blood glucose is fast and simple, and is more economical than existing methods. The cost to patients of such a method would be significantly less over time than existing methods because only a monitor 10 would be required, and the high monthly expense of testing strips would be avoided. In addition, patient acceptance would be very high because of the non-invasive nature and the simple use of the procedure.

In addition, the present invention produces improved spatial resolution since the effect only occurs in regions of space where the magnetic field distribution can be precisely controlled. Improved signal to noise ratio can also be achieved due

to an AC modulation of the desired signal which can be detected using a lock in amplifier for phase coherent detection. This lock-in technique can actually pull a signal out of over 100 db of additive random noise. Further, the magnetic field (B) provided about the cell 14 of glucose solution eliminates the cancellation of the conventional optical rotation effect that occurs upon reflection from a dielectric [E field inverting] mirror 16. This makes possible glucose measurements after reflection from the aqueous/lens interface.

While the present invention has been described to determine the blood glucose level of an individual, one will appreciate that this could also be useful in glucose detection in biotechnology applications, where non-invasive methods to determine the concentration of glucose in a solution is required.

Although the foregoing detailed description has been directed to the measurement of glucose in the aqueous humor 34, the apparatus and method are adaptable to other applications where an optically active substance is to be measured. As one example, some biogenetic processes have optically active materials either as reactants or products, and the apparatus and method may be used as a non-invasive tool to follow the progress of the reaction without the potential for contamination presented by sampling devices.

It will be understood that a person skilled in the art may make modifications to the preferred embodiment shown herein within the scope and intent of the claims. While the present invention has been described as carried out in a specific embodiment thereof, it is not intended to cover the invention broadly within the scope and spirit of the claims.

CLAIMS

What is claimed is:

1. A method for measuring the concentration of a material in the aqueous humor of an eye, comprising:

generating a beam of polarized light from a light source;

directing said beam into an eye of a subject along a light path such that the beam reflects from an interface in the eye and returns from the eye back towards the light source;

applying a modulated gyrotropic field to the aqueous humor of the eye which gyrotropic field is effective to produce an alteration in the polarization of the light passing through the aqueous humor in the field which alteration may be represented as $\delta = Bxf(C_m)xd$, where δ is the alteration in polarization, B is the field strength, C_m is the concentration of the material, $f(C_m)$ is a function of the said concentration, and d is the distance traversed to produce a modulated alteration in the polarization of the reflected beam of light related to the intensity of the gyrotropic field and the dependence of said function $f(C_m)$ on the concentration of said substance within the aqueous humor;

receiving the reflected beam of light and detecting said modulated variation in polarization; and

determining the concentration of said substance from said alteration in polarization produced by said field dependent on the concentration related value of the function $f(C_m)$.

2. A method as claimed in claim 1, wherein the gyrotropic field is a magnetic field and $f(C_m)$ is the concentration dependent value of the Verdet constant of the aqueous humor.

3. A method as claimed in claim 2, wherein the magnetic field is generated by applying an alternating electrical voltage to a coil positioned adjacent the eye.

4. A method as claimed in claim 2, wherein the magnetic field is produced by a permanent magnet which is shifted in position to produce said modulation of the field.

5. A method as claimed in claim 2, wherein the magnetic field is produced by a permanent magnet provided with a moveable shield which shields the aqueous humor from the magnetic field to a degree dependent on the position of the shield, and wherein the shield is moved to modulated said magnetic field.

6. A method as claimed in claim 1, wherein the light source is a laser.

7. A method as claimed in claim 1, wherein the light source is a non-temporally coherent light source.

8. A method as claimed in claim 1, wherein said interface is the anterior surface of the lens of the eye.

9. Apparatus for optically measuring the concentration of an optically active material in the aqueous humor of an eye, comprising

a light source generating a beam of polarized light;

said source being mounted to direct said beam into an eye of a subject along a light path such that the beam reflects from the anterior surface of the lens of the eye and returns from the eye towards the light source;

a source of a modulated gyrotropic field adapted to be located sufficiently close to the aqueous humor of the eye to produce a modulated alteration in the polarization of the beam of light;

which gyrotropic field is effective to produce an alteration in the polarization of the light passing through the aqueous humor in the field which alteration may be represented as $\delta = Bxf(C_m)xd$, where δ is the alteration in polarization, B is the field strength, C_m is the concentration of the material, $f(C_m)$ is a function of the said concentration, and d is the distance traversed to produce a said modulated alteration in the polarization of the reflected beam of light related to the intensity of the gyrotropic field and the dependence of said function $f(C_m)$ on the concentration of said substance within the aqueous humor;

an optical detector for receiving the reflected beam of light and detecting said modulated alteration in polarization; and

computation apparatus for determining the concentration of said substance from said alteration in polarization produced by said field dependent on the concentration related value of the function $f(C_m)$.

10. Apparatus as claimed in claim 9, wherein the source of the gyrotropic field is a magnetic field source and the function $f(C_m)$ is the concentration dependent Verdet constant of the aqueous humor.

11. Apparatus as claimed in claim 10, wherein the magnetic field source comprises a coil adapted to be positioned adjacent the eye, said coil being connected to a source of alternating electrical voltage.

12. Apparatus as claimed in claim 10, wherein the source of magnetic field comprises a permanent magnet mounted for movement to produce said modulation of the field.

13. Apparatus as claimed in claim 10, wherein the source of magnetic field comprises a permanent magnet provided with a moveable shield which shields the aqueous humor from the magnetic field to a degree dependent on the position of the shield, and wherein the shield is mounted for movement to modulate said magnetic field.

14. Apparatus as claimed in claim 9, wherein the light source is a laser.

15. Apparatus as claimed in claim 9, wherein the light source is a non-temporally coherent light source.

16. Apparatus as claimed in claim 9, wherein the said source of modulated gyrotropic field modulates said field at a first frequency and the apparatus further comprises a gyrotropic polarization modulator modulating the light reaching the optical detector at a second frequency.

17. Apparatus as claimed in claim 16, further comprising a lock in amplifier connected to receive as inputs an output signal from the optical detector and the modulation of the gyrotropic polarization modulator and producing an output which is connected to form a phase and frequency locked loop controlling the modulation of the polarization by the gyrotropic polarization modulator and to provide phase and frequency locked detection of the concentration dependent alteration in polarization produced by the gyrotropic field applied to the aqueous humor.

18. Apparatus as claimed in claim 17, further comprising a second lock in amplifier connected to receive as inputs the output from the first said lock in amplifier and the modulation of said gyrotropic field acting on the eye and to produce an output providing phase and frequency locked detection of the output signal of the first lock in amplifier providing a measurement of the alteration of the polarization of the light produced by said modulated gyrotropic field resulting in an improved signal to noise ratio.

19. An apparatus for determining the concentration of an optically active substance in a solution, the apparatus comprising:

a light source for producing a beam of light arranged to direct said beam of light to pass through a least a portion of said solution;

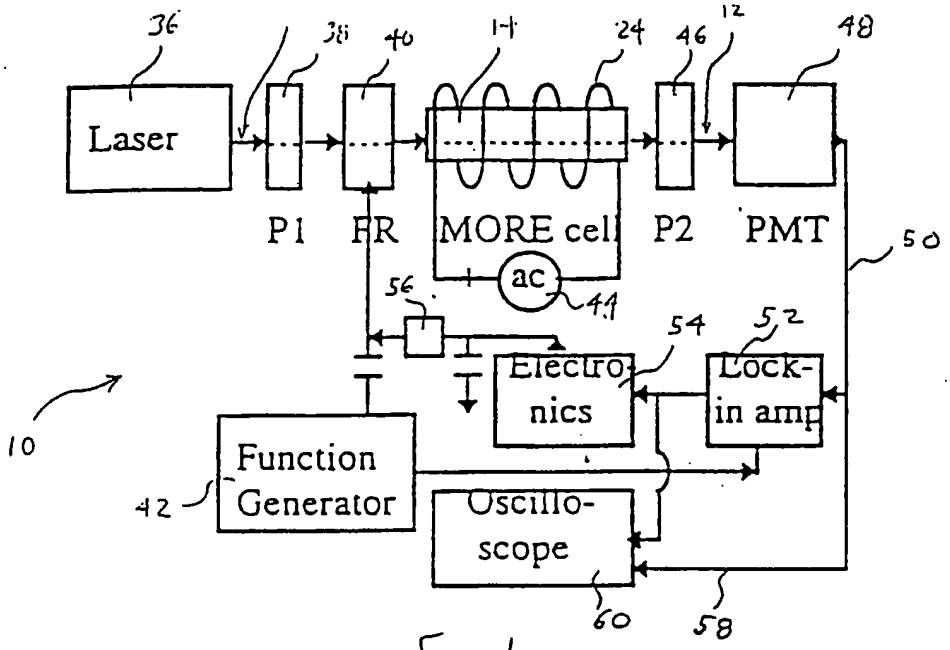
a source of magnetic field applied to at least said portion of the solution;

an optical reflector arranged with respect to said light source and said solution so as to reflect said beam of light to re-pass through at least said portion of said solution;

an optical detector for receiving said beam of light after said re-passage through the solution, the optical detector providing an output signal indicative of the optical rotation of the solution in the presence of the magnetic field.

20. A method for measuring the concentration of a substance in a solution, comprising measuring magneto-optical rotation produced in said solution, which rotation is indicative of the concentration dependent Verdet constant of the solution, and obtaining said concentration therefrom.

21. A method as claimed in claim 20, wherein the light is reflected to pass twice through said solution and the magneto-optical rotation produced by said double passage is detected.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38
40
14
24
46
12
48
Laser
P1
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P2
PMT
50
ac
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Electro-
nics
Lock-
in amp
10
Function
Generator
42
Oscillo-
scope
60
58

Fig. 1

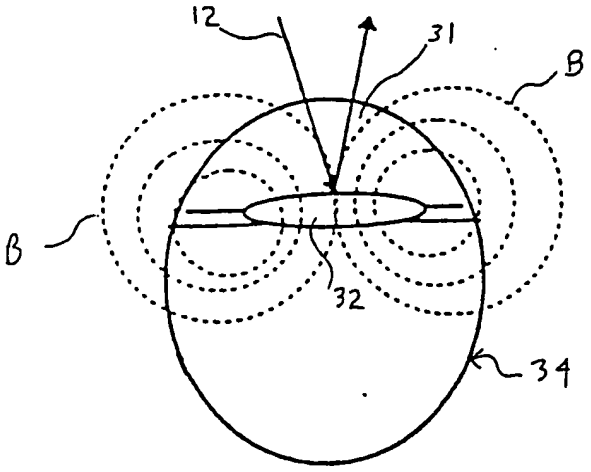

12
31
B
B
32
34

Fig. 4

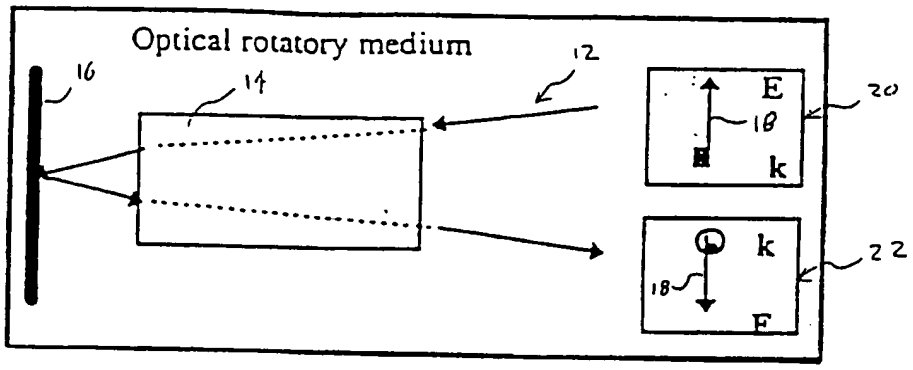
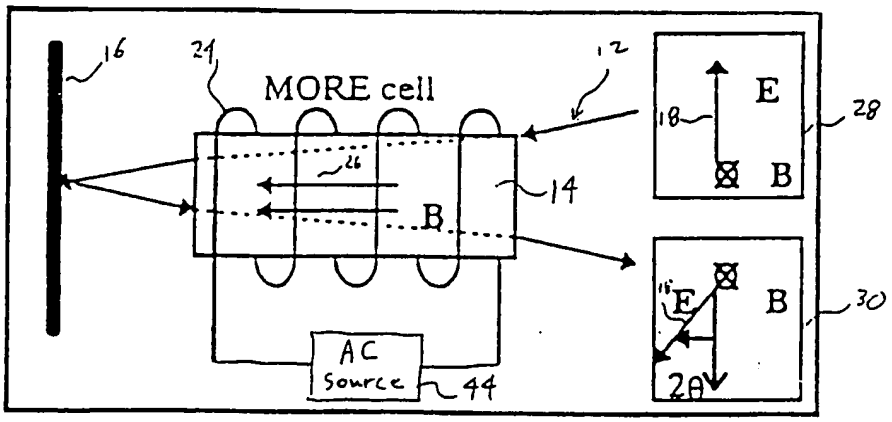

Optical rotatory medium
16
14
12
E
18
k
20
k
18
E
22

Fig. 2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B
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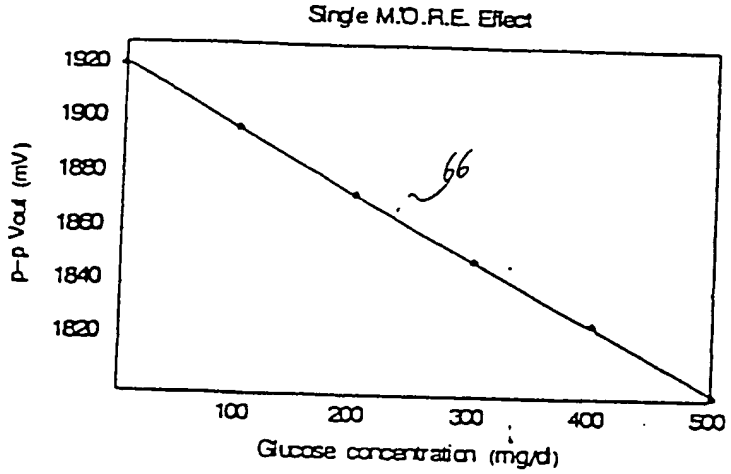
18
B
30
AC
Source
44
2θ

Fig. 3


Single M.O.R.E. Effect
1920
1900
1880
1860
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1820
P-p Vout (mV)
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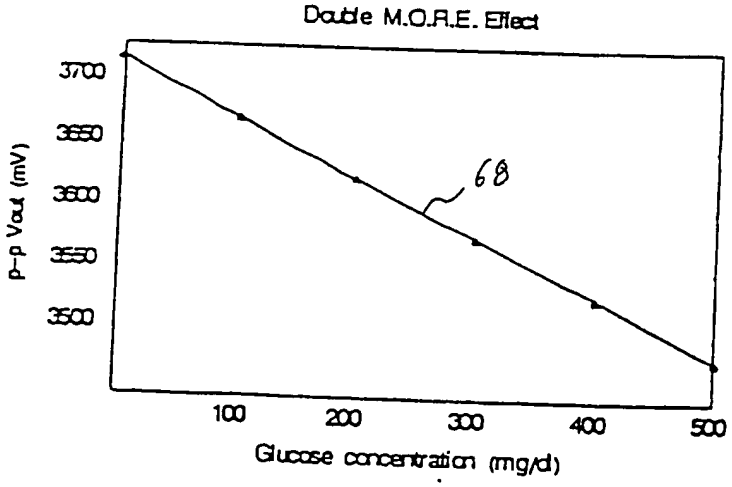
100
200
300
400
500
Glucose concentration (mg/dl)

Fig. 5


Double M.O.R.E. Effect
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3500
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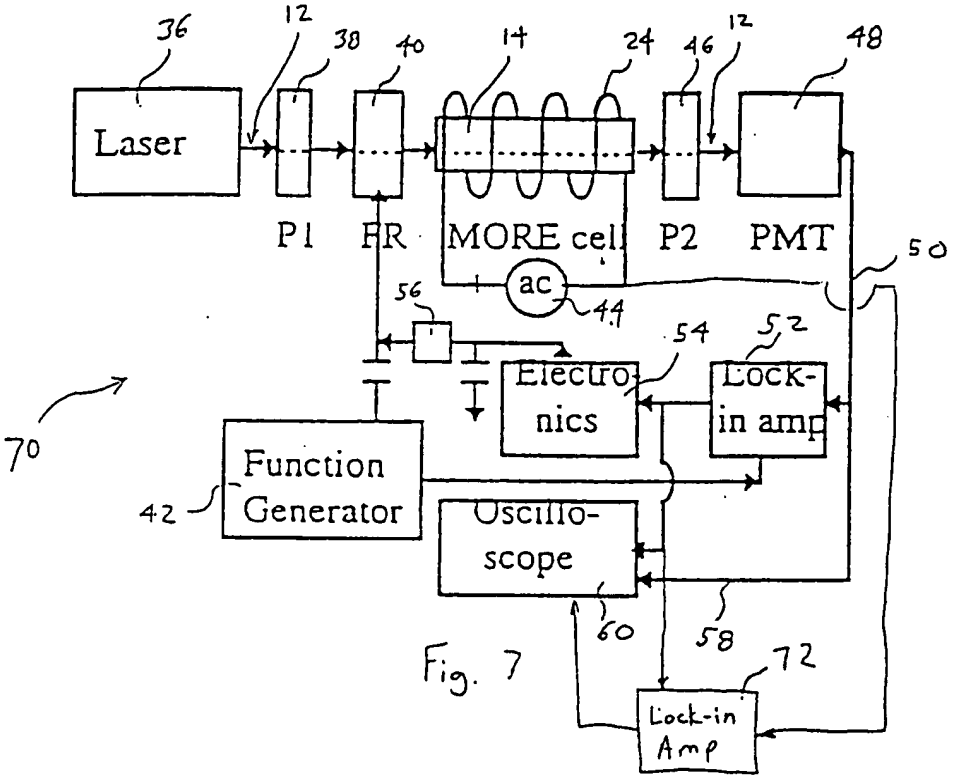
100
200
300
400
500
Glucose concentration (mg/dl)

Fig. 6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14
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46
12
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P1
FR
MORE cell
P2
PMT
50
ac
44
56
54
52
Electro-
nics
Lock-
in amp
70
Function
Generator
42
Oscillo-
scope
60
58
72
Lock-in
Amp

Fig. 7

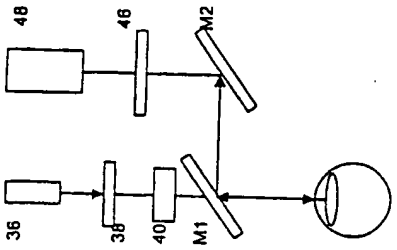

FIG. 8

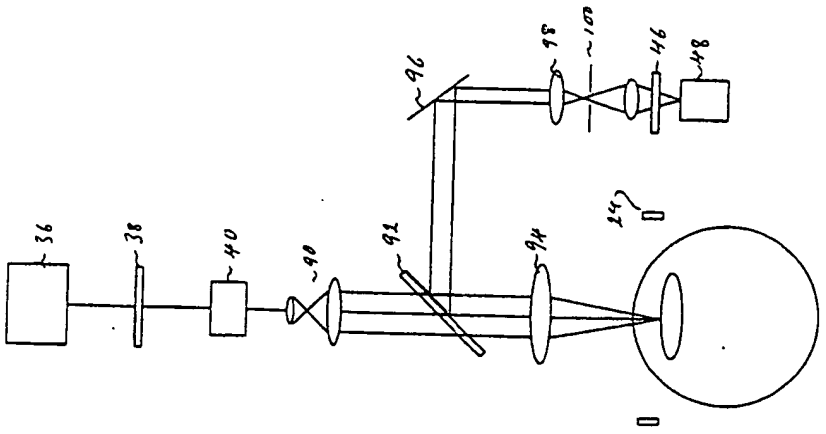

Fig 9.

INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/US 00/26659

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/00 G01N21/21

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B G01N G01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, INSPEC, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JANG SUNGHOON AND FOX MARTIN D.: "Double Lock-in Concept for MORE Clucose Detection" PROCEEDINGS OF THE IEEE 25TH ANNUAL NORTHEAST BIOENGINEERING CONFERENCE (CAT. NO. 99CH36355) WEST HARTFORD, CT, USA, 8 - 9 April 1999, pages 122-124, XP002155401 section "Methods" and "Discussion" --- -/--	1-3,6, 8-11,14, 16-21

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 December 2000	15/01/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Knüpling, M

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INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/US 00/26659

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	BROWNE A F ET AL: "MICRODEGREE POLARIMETRIC MEASUREMENT OF GLUCOSE CONCENTRATIONS FOR BIOTECHNOLOGY APLLICATIONS" PROCEEDINGS OF THE IEEE NORTHEAST BIOENGINEERING CONFERENCE,US,NEW YORK, IEEE, vol. CONF. 23, 21 May 1997 (1997-05-21), pages 9-10, XP000738103 ISBN: 0-7803-3849-9	20
A	the whole document	1,2,6, 9-11,14, 16,17,19
A	EP 0 902 270 A (MATSUSHITA ELECTRIC IND CO LTD) 17 March 1999 (1999-03-17) page 2, line 8 - line 12 page 6, line 5 - line 30 page 7, line 10 - line 49	1-6, 9-14,16, 17,19,20
A	WO 97 34521 A (ABBOTT LAB) 25 September 1997 (1997-09-25) page 14, line 19 -page 15, line 28 page 8, line 4 - line 5	1,6-9, 14,15, 17,19

1

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Interna[illegible]nal Application No
PCT/US 00/26659

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		JP 11094732 A	09-04-1999
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		CN 1215162 A	28-04-1999
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		JP 2000507349 T	13-06-2000